

REMARKS/ARGUMENTS

Applicant thanks the Examiner for the interview conducted on December 22, 2004 in which the 35 U.S.C. §103(a) rejections to independent claims 31 and 37 were discussed. Both the Papac references and the Gaskell reference were discussed in detail. As a result of that interview, Applicants have amended independent claims 31 and 37 for further consideration. After entry of the foregoing amendments, claims 31-33, 35-40, 42, 44-46 and 48 (2 independent claims; 14 total claims) remain pending in the application. Reconsideration is respectfully requested.

Claims 31-33, 35, 36-40 and 42 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac (Analytical Chemistry) in view of Gaskell. In particular, the Examiner states that Papac discloses a method for the mass spectral identification and detection of analytes separated by amino affinity chromatography. The Examiner further states that Papac discloses antibody immobilized to agarose beads and used as affinity columns and that Papac combines a specimen with beads to capture antigen present in the sample. The Examiner further states that Papac discloses washing to remove any unbound antigen and that the sample is mixed with the beads and centrifuged and that the supernatant is removed. Finally, the Examiner states that Papac discloses that a matrix containing formic acid was added and the supernatant was tested by MALDI/TOF mass spectrometry and that the analyte is determined by mass-to-charge ratio. Although the Examiner concedes that Papac differs from the instant invention by failing to teach that the specimen is combined with an internal reference species of known concentration prior to the capturing and isolation steps where both the analyte and the IRS are captured and isolated, the Examiner contends that Gaskell discloses the addition of an internal reference standard to a specimen containing analytes and determining the analyte by mass spectrometry. The Examiner further states that Gaskell discloses capturing and isolating the analyte and internal standard with an affinity reagent and that a standard curve is used for the quantitation of the analyte and internal standard. The Examiner also contends that Gaskell discloses that the standard curve was established by analysis of derivatized standard mixtures and that the addition of the internal standard to the specimen provides higher precision to the analytical procedures. The Examiner also stated that Gaskell discloses that the immunoadsorption technique provides a rapid and convenient procedure for an analyte before analysis. In conclusion, the Examiner stated that it would have been obvious to one of ordinary skill in the art to incorporate an internal standard

and affinity reagent as taught by Gaskell into the method of Papac because Gaskell teaches that the addition of the internal standard to the specimen provides higher precision to the analytical procedures and also teaches that the immunoadsorption technique provides a rapid and convenient procedure for an analyte before analysis. Applicants respectfully traverse this rejection.

As discussed in the interview with the Examiner, the Papac (Analytical Chemistry) reference fails to disclose quantifying the amount of one or more analytes using only mass spectrometry. Papac also fails to disclose using mass spectrometry for identifying an unknown analyte as claimed by the instant application in that the analyte which is analyzed in Papac is already known. (See Declaration of Randall W. Nelson). In addition, the Gaskell reference teaches away from the instantly claimed invention by using tandem MS for quantification. In Gaskell, the analyte and IRS are not measured using MS in a single measurement. The Gaskell reference also teaches away from the instant claimed invention by requiring multiple sample preparation steps in between extraction and mass spectrometry. (See Declaration of Randall W. Nelson.) Finally, it should be noted that the prior art references that have been cited in the prosecution of this application have used dual forms of separation. For example, the 1990 Gaskell reference uses mass spectrometry as a separation step followed by mass spectrometry for mass detection. In another example, the 1983 Gaskell et al. reference (Clinical Chemistry) utilizes gas chromatography as a separation step which is then followed by mass spectrometry for mass detection. The instant application involves performing separation and detection in one mass spectrometric step. The identification and quantification of an analyte is determined using only single dimension mass spectrometric analysis. Dual forms of separation are not utilized. (See Declaration of Randall W. Nelson.) Therefore, it would not have been obvious to one of ordinary skill in the art to incorporate the internal standard and affinity reagents taught by Gaskell into the method of Papac to arrive at Applicants' claimed invention.

Claims 44-46 and 48 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Papac (Analytical Chemistry) and Gaskell in view of Merren. The Examiner states that Papac and Gaskell differ from the instant invention in failing to specifically teach interpolating the analyte species' mass spectrometric response to the IRS's mass spectrometric response. The Examiner further contends that Merren teaches the addition of reference substance which provides a spectrum containing peaks at several known mass-to-charge ratios. The Examiner further contends that Merren teaches that this reference spectrum is accurately correlated with

the spectrum of the unknown substance and that the reference peaks act as accurate markers forming a calibrated scale from which the mass-to-charge ratios of peaks of the unknown substance is interpolated. The Examiner further states that Merren teaches that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances thereby permitting single channel processing of the combined signal. Therefore, the Examiner contends that it would have been obvious to one of ordinary skill in the art to interpolate the analyte species and the reference species as taught by Merren into the modified method of Papac because Merren shows that this provides a method for combining signals representative of the simultaneous spectral analysis of two substances thereby permitting single channel processing of the combined signal. Applicants respectfully traverse this rejection.

As previously discussed above, the combination of Papac and Gaskell would not be obvious to one of ordinary skill in the art. In addition, Merren fails to disclose separation and detection in one mass spectrometric step and also fails to disclose identification and quantification of an analyte using only single dimension mass spectrometric analysis. Therefore, it would not be obvious to one of ordinary skill in the art to further combine Merren with Papac and Gaskell to arrive at Applicants' claims 44-46 and 48.

In view of the foregoing, Applicants respectfully submit that all of the pending claims are allowable over the prior art of record. Reconsideration of the application and allowance of all pending claims is earnestly solicited. Should the Examiner wish to discuss any of the above in greater detail or deem that further amendments should be made to improve the form of the claims, then the Examiner is invited to telephone the undersigned at the Examiner's convenience. The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment, to Deposit Account No. 19-2814. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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